

## METHODS FOR REGULATING GENE EXPRESSION

### Abstract

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Methods of regulating gene expression in subjects using tetracycline-responsive fusion proteins are disclosed. In one embodiment, the method involves introducing into a cell the subject a nucleic acid molecule encoding a fusion protein which inhibits transcription, the fusion protein comprising a first polypeptide which binds to a *tet* operator sequence, 10 operatively linked to a heterologous second polypeptide which inhibits transcription in eukaryotic cells; and modulating the concentration of a tetracycline, or analogue thereof, in the subject. The first polypeptide can binds to a *tet* operator sequence in the absence, but not the presence, of tetracycline. Alternatively, the first polypeptide can binds to a *tet* operator sequence in the presence, but not the absence, of tetracycline. In another embodiment, the 15 method of the invention involves obtaining a cell from a subject, introducing into the cell a first nucleic acid molecule which operatively links a gene to at least one *tet* operator sequence, introducing into the cell a second nucleic acid molecule encoding an inhibitory fusion protein of the invention to form a modified cell, administering the modified cell to the subject and modulating the concentration of a tetracycline, or analogue thereof, in the subject. 20 The first and second nucleic acid molecules can be linked or can be separate molecules.